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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,304	12/28/2001	Jonathan A. Ellman	045413/0110	3985

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EXAMINER	
EPPERSON, JON D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 11/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,304	ELLMAN ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53 and 67-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53 and 67-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/20/06 has been entered. Claims 53, 65 and 66 were pending. Applicants added claims 67-89 and canceled claims 65 and 66. In addition, claim 53 was amended. Therefore, claims 53 and 67-89 are currently pending and examined on the merits (e.g., see 8/31/06 Response, page 2, paragraph 1, "applicants note that all of the new claims 67-89 read on the elected species").

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Priority

2. Applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § 120 as follows:

This application is a CON of 09/277,461 filed 3/26/1999 (now US PAT 6,344,334), which is a CIP of 09/049,754 filed 3/27/1998 (now US PAT 6,344,330). However, one or more of the applications upon which priority is based fail to provide adequate support under 35 U.S.C. § 112, first paragraph for the claims of this application.

(A) For ***claims 53 and 67-89***, both the '754 and '461 applications fail to provide support for the use of the currently claimed compounds of CTBF-S-S-R^8 as set forth in independent claim 53 or fragment-S-S-R^8 as set forth in independent claim 78 (see also New Matter rejections, which are incorporated in their entirety herein by reference).

Therefore the effective filing date for claims 53 and 67-89 is deemed to be the filing date of the present application, **December 28, 2001**.

Withdrawn Objections/Rejections

3. The Kirkpatrick rejection under 35 U.S.C. § 103(a) is withdrawn in view of Applicants' arguments, the Kruger 132 declaration and the evidence submitted, especially exhibit 9 stating in most instances -NH_2 will not be an isosteric substitution for –OH and/or halogen (see especially page 303, "General conclusions to class 1"; see also Table 1). All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 112, first paragraph

4. Claims 53 and 67-89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicants' newly amended claims are directed to a broad genus of candidate target binding fragments (CTBF's) and/or just plain fragments (as set forth in newly

added independent claim 78). Although Applicants' claims have been amended to recite "small" molecules that are "sufficiently soluble" to be test, the claimed CTBF's still read on virtually an infinite number of compounds because Applicants' do not limit the way in which the organic atoms can be arranged to form the claimed compounds. Furthermore, Applicants admit that their claimed compounds read on at least 600,000+ compounds as set forth in "typical" pharmaceutical archives and as sold by various commercial vendors (e.g., see 4/20/06 Response, page 11, paragraphs 1 and 2). In addition, Applicants do not specify any target molecule or method of testing (e.g., see 35 U.S.C. § 112, second paragraph "metes and bound" rejection; see also 4/20/06 Response, page 11, section E, "E. Binding Properties Would not Have Had to be Known A Priori in order for the Skilled Artsian to Recognize the Claimed Library").

In contrast, Applicants' specification provides only one working example of a CTBF drawn to a cross-linked oxime library that inhibits the interaction between gp120 and CD4 (e.g., see specification, pages 76-84, Example 1, see also figures 2 and 4 wherein the aldehyde precursors to the oxime library are disclosed).

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the claimed invention (e.g., see *In re Edwards*, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978); see also see also *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111 (CAFC 1991)). The "written description" requirement may be satisfied by using "such descriptive means as words, structures, figures, diagrams formulas, etc., that fully set forth the claimed invention" (e.g., see *Lockwood*, 107 F.3d at 1572, 41 USPQ2d

at 1966). In the present case, Applicants' specification provides only one example of a cross-linked oxime library that inhibits the interaction between gp120 and CD4 (see above). In addition, when there is *substantial variation within the genus*, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05). Here, the variation within the genus would be enormous because the nature of the claimed compounds would depend on a vast number of undefined biological target molecules that do not share any common properties and the method of undefined solubility testing techniques (e.g., see 35 U.S.C. § 112, second paragraph rejections below). Therefore, Applicants' one example does not adequately support the virtually unlimited number of currently claimed compounds and/or their use. For example, Lauf et al. state, "The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored" (e.g., see U.S. Patent Application No. 2004/0062911 A1, page 1, paragraph 4). In addition, Young et al. state, "For a given [combinatorial] reaction or sequence of reactions, the number of possible products can be astronomical ... it is impossible to make all possible products. Even with a two-component reaction with a modest number of building blocks, it generally does not make economic sense to build all the products, as there may be more than can be afforded and many may be largely redundant" (see Young et al., "Design of

Diverse and Focused Combinatorial Libraries Using an Alternating Algorithm" *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 1916-1921, especially page 1916, column 1, paragraphs 1 and 2).

Here, by analogy to Lauf et al. and Young et al. above, Applicants do not limit the 100 elements that can be used with the exception that "carbon" must be one of those elements (i.e., an "organic" molecule). In addition, Applicants do not limit the number of elements (i.e., three, four, five, six) element that can be combined together to form said CTBFs and/or fragments. Therefore, it is clear that Applicants' have not made, nor have they used, nor have they even envisioned, the vast majority of compounds that they are currently claiming.

The CAFC has also stated that a "written description on an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." (e.g., see *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993)). Here, Applicants have failed to provide a definition, structure, formula or chemical name for any of the compounds that fall within the scope of a CTBF with the exception of the oxime library. The CAFC has stated that a genus, which is set forth only in functional terms, "... is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function" (e.g., see *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (1997)). Here, Applicants claim CTBF's that can only be distinguished from other compounds by their

function (i.e., their ability to act as a candidate target binding fragment or their ability to be "sufficiently soluble" to permit detection), which was held to be impermissible in *Lilly*. Just as the generic term "cDNA" did not provide an adequate written description for the broad class of mammalian or vertebrate insulin DNA in *Lilly*, neither does the generic term "CTBF" or "fragment" provide an adequate written description for the broad class of currently claimed compounds because the term "CTBF" and/or "fragment" only defines what the compound does (e.g., it ability act as a candidate target binding fragment or its ability to dissolve in water) rather than what the compound is (e.g., a chemical formula). In fact, this case is even more egregious than *Lilly* because there is no "genetic code" to correlate the CTBF with a related molecule and/or target or the fragment with its related solubility when referenced to some undefined technique for measuring said solubility.

Thus, applicants have not demonstrated in "full, clear, concise, and exact terms" that they are in possession of the claimed invention. It is well settled that claiming only a result (e.g., ability to act as a candidate target) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result (i.e., every conceivable "small", "water soluble" library), far beyond those means actually discovered or contemplated by the inventor (i.e., oxime library), so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217; *Siegel v. Watson*, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119.

Response

5. Applicant's arguments directed to the above written description rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "All of the library members of claim 53 have the distinguishing chemical structure CTBF-S-S-R8, which is describe in the specification. All of the library members have the -SS-, R moiety, which is a chemical formula" (e.g., see 4/20/06 Response, page 8, paragraph 2).

[1] The SS and R moiety are not at issue in this rejection. Therefore, Applicants' arguments are moot. The Examiner has only alleged that the CTBF portion of the molecule fails the test.

[2] Applicants argue, "The attached 132 Declaration by Dr. Clinton Kruger (Exhibit 1) provides direct evidence, that a person of skill in the art does indeed recognize that the applicants invented what is claimed. In this Declaration, Dr. Kruger states that he 'find[s] the claimed library sufficiently described in paragraphs 148 (general description of R8) and 221 (general description of the disulfide containing library) ..." (e.g., see 4/20/06 Response, page 8, paragraph 3 and 4; see also Declaration by Dr. Kruger).

[2] The Declaration under 37 CFR 1.132 filed 4/20/06 is insufficient to overcome the rejection of claims 53 and 67-89 based upon 35 U.S.C. § 112, first paragraph as set forth in the last Office action (and above) because Applicants' arguments are not commensurate in scope with the claims. The issue isn't whether the SS or R moiety are adequately described but, rather, whether the CTBF or fragment portion of the molecule is adequately described. Therefore, the declaration and arguments are not on point. In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

[3] Applicants argue, "The Lilly facts are not Analogous to the Present Application ... In contrast [to Lilly], the present invention relates to a combinatorial library, which is used to assay large numbers of compound to determine their binding to a particular target. Whether or not a CTBF-S-S-R^8 compound binds to a target, it has provided useful information. Either a negative result or a positive results provides useful information for scientific research related to the CTBF-S-S-R^8 and its target. This contrasts sharply to precision required for a nucleotide sequence to be translated into a biologically functional coding sequence [as in Lilly]" (e.g., see 4/20/06 Response, page 9 and 10).

[3] The Examiner respectfully disagrees. While it may be true that a library member may provide useful information whether a positive or negative result is the same, the library members must still possess certain physical characteristics to fit within the umbrella of a "candidate target binding ligand" separate and distinct from any other ligand that might be employed. Otherwise the term "candidate target binding" would be rendered meaningless or, alternatively, superfluous.

Furthermore, what separates a "candidate target binding fragment" from an common ordinary fragment is less than clear (e.g., see 35 U.S.C. § 112, second paragraph rejection below). Therefore, use of the term "candidate target binding fragment" is even more egregious than Lilly because there is no "genetic code" to correlate the CTBF with a related molecule and/or target (or the fragment with its related solubility) especially when the correlation depends on an ambiguous function.

Furthermore, the Examiner is unaware of any per se rule that all libraries are adequately defined under 35 U.S.C. § 112, first paragraph because both "negative" and "positive" results are useful. Applicants must still show possession of the claimed invention and setting forth one example to allegedly support virtually an infinite number of possibilities, as is the case here, fails to achieve this goal. It is well settled that claiming only a result (e.g., ability to act as a candidate target) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result (i.e., every conceivable library), far beyond those means actually discovered or contemplated by the inventor (i.e., oxime library), so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217; *Siegel v. Watson*, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119.

Finally, The prior art also indicates that not all libraries are created equal and that a person of skill in the art cannot predict whether "useful" results can be obtained by screening any given library. For example, Muegge states, "the success rate of these early random libraries is considered to be low. The somewhat disappointing performance can be attributed, for example,

to the high flexibility of synthesized molecules as well as to their high lipophilicity. In addition, the libraries were often limited in their pharmacophore diversity ... For receptor and enzyme targets, on average one lead compound is identified for 120,000 compounds screened. HTS is much less successful for targets of protein protein interaction" (e.g., see Muegge, "Pharmacophore Features of Potential Drugs" Chem. Eur. J. 2002, 8, No. 9, pages 1977-1981, especially page 1977, column 1, paragraph 1). In addition, this "disappointing" success rate is further plagued by "false positives" that "inflate" the true hit rate. For example, McGovern et al. state, "screening hit lists [i.e., libraries] continue to be populated, even dominated, by compounds that act with atypical properties that cannot be described by any existing model; such compounds are unlikely to be pharmaceutically useful" (e.g., see McGovern et al., "A Common Mechanism Underlying Promiscuous Inhibitors from Virtual and High-Throughput Screening" *J. Med. Chem.* **2002**, *45*, 1712-1722, especially page 1712, column 2, paragraph 1; see also page 1720, column 2, paragraph 2, "such nonspecific inhibitors would artificially inflate hit rates in screening for new drug leads. Much effort can be wasted chasing [these compounds] ... that are unlikely to be useful biologically"). This is also confirmed by Gilllet et al. state, "early results from combinatorial libraries were disappointing with libraries either failing to deliver the improved hit rates that were expected or resulting in hits that did not have "druglike" characteristics. Thus, it is now evident that diversity alone is an insufficient criterion for library design and other factors should also be taken into account. For example, the physicochemical properties of the molecules that determine effects such as ADME are important as well as other factors such as cost and availability of reactants. Consequently, the focus in combinatorial library design has now shifted toward designing libraries based on a number of properties

Genetic Algorithm" J. Chem. Inf. Comput. Sci. 2002, 42, 375-385, especially page 375, column 1). Thus, not all combinatorial libraries are considered to be "useful" as purported by Applicants.

[4] Applicants argue, "The Present Claims do Recite Identifying Chemical Structures and Physical Properties ... the CTBFs are defined by physical characteristics (small, organic and water soluble) ... The court in Lilly opined that 'the name cDNA . . . conveys no distinguishing information' and 'there is no further information in the patent pertaining to that cDNAs relevant structural or physical characteristics.' The facts of Lilly do not square with the present claims, which do have distinguishing information, and the specification, which does disclose relevant structural and physical characteristics"

[4] The Examiner respectfully disagrees. The characteristics referred to by Applicants are indefinite at best (e.g., see 35 U.S.C. § 112, second paragraph rejection below) and, as a result, Applicants' arguments are moot. Furthermore, the "size" of the molecule and its "solubility" would not distinguish a "candidate target binding" fragment from any other fragment. Therefore, Applicants' alleged "distinguishing" characteristics are not actually useful in this regard as erroneously purported.

[5] Applicants argue, "applicants have provided examples of 29 species of possible CTBFs" and presumably as a result are adequately described (e.g., see 4/20/06 Response, page 10, last full paragraph).

[5] These is no evidence that any of these molecules where actually tested in the present

invention. Applicants provide only one working example of a CTBF drawn to a cross-linked oxime library that inhibits the interaction between gp120 and CD4 (e.g., see specification, pages 76-84, Example 1, see also figures 2 and 4 wherein the aldehyde precursors to the oxime library are disclosed). Furthermore, simply listing four classes of known compounds does not support the infinite number that is currently be claimed because these prophetic examples are not commensurate in scope with the claims.

[6] Applicants argue, "Combinatorial Chemical Libraries were Known in the Art as of the Filing Date ... which contrasts with the facts of Lilly where there were no known insulin cDNA sequences in the prior art" (e.g., see 4/20/06 Response, page 10, last paragraph).

[6] When there is little to no disclosure in the instant specification of the starting material or conditions under which claimed process can be carried out, this failure cannot be rectified by asserting that all disclosure related to the process is within skill of art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997). Here, Applicants provide only one working example of a CTBF drawn to a cross-linked oxime library that inhibits the interaction between gp120 and CD4 (e.g., see specification, pages 76-84, Example 1, see also figures 2 and 4 wherein the aldehyde precursors to the oxime library are disclosed). Thus, simply drawing out a laundry list of known compounds or referring to prior art recitations of known libraries does not cure the deficiencies noted above.

[7] Applicants argue, "For instance ... applicants have indicated in the specification that commercial catalogs are handy sources of CTBFs. As noted in the attached pages from Delvin 1997, (Exhibit 6) the Aldrich chemical company (mentioned at pagraph [0073] of the present

application) 'drew upon 30,000+ compounds' available as test compounds for combinatorial libraries. Eleven other commercial suppliers of compound libraries are mentioned, with tens of thousand, even 400,000 structures available for libraries. Moreover, according to Dolle, Journal of Combinatorial Chemistry, by the year 1998, 683 combinatorial libraries were publicly 'abstracted along with their generic structures' in the review series published by this jomal. Examples of the libraries are detailed in the Dolle article. Moreover, Terret 1998 (Exhibit 7) states that '[t]he average pharmaceutical company archive contains in the region of 200,000 compounds.'" (e.g., see 4/20/06 Response, page 11, paragraphs 1 and 2). That is, Applicants argue that all libraries are necessarily described as a matter of law under 35 U.S.C. § 112, first paragraph (i.e., a *per se* rule) because all compounds can be screened because whether a particular compound binds to a given target or not still provide useful "positive" or "negative" results.

[7] The Examiner is unaware of such a *per se* rule holding all libraries to be adequately described as a matter of law. To the contrary, a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species (e.g., see Fujikawa v. Wattanasin, 93 F.3d 1559,1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967)). Thus, simply referring to the 200,000+ compounds in the archives of a "typical" pharmaceutical company (which Applicants may not have had access to at the time of filing) or the 400,000+ compounds sold by the 11 commercial venders or even all known compounds in the universe (if Applicants' arguments were allowed to balloon to this level) would not reasonably lead a skilled artisan to any particular species. That

is, Applicants provide no starting point or guidance that would allow a skilled artisan to narrow down this enormous laundry list to a set of useful compounds. This amounts to nothing more than trial and error research, which is impermissible (e.g., see *University of Rochester v. G.D. Searle & Co., Inc.* 69 USPQ2d 1886, 1889 (CAFC 2004)) (holding a patent drawn to a method for inhibiting PGHS-2 enzymatic activity invalid for failure to meet the written description requirement because said patent "... neither disclose[d] any such compound nor provide[d] any suggestion as to how such a compound could be made or otherwise obtained other than by trial-and-error research"). For example, Lauf et al. state, "The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored" (e.g., see U.S. Patent Application No. 2004/0062911 A1, page 1, paragraph 4). Here, by analogy to Lauf et al., Applicants do not limit the 100 elements that can be used with the exception that "carbon" must be one of those elements (i.e., an "organic" molecule). In addition, Applicants do not limit the number of elements (i.e., three, four, five, six) element that can be combined together to form said CTBFs and/or fragments. Therefore, it is clear that Applicants' have not made, nor have they used, nor have they even envisioned, the vast majority of compounds that they are currently claiming.

[8] Applicants argue, "Binding Properties Would not Have Had to be Known A Priori in order for the Skilled Artisan to Recognize the Claimed Library ... The real issue is not whether

one of the skill in art would know binding properties a priori but whether one of skill in the art would be able to recognize a library of small organic molecules, all with the S-S-R^8 moiety. A 'candidate' target binding fragment is only a fragment that might potentially bind to a target. Candidates are selected for assaying against biological molecules in accordance with what the target biological molecule is and the strategy behind the assay. If those of skill in the art knew in advance what binding fragment would bind to a biological molecule, there would be no need for libraries of compounds to assay against target molecules. In other words, it is the very nature of combinatorial libraries that the binding.properties will not be known with certainty in advance. Hence, the use of the term "candidate" to modify target binding fragment" (e.g., see 4/20/06 Response, page 11, last two paragraphs).

[8] The Examiner respectfully disagrees. Again the SS-R8 portion of the molecule is not at issue in this case. Attaching a known compounds to a chemical moiety that is not adequately supported does not alleviate these deficiency in that portion that is not adequately described. Furthermore, the fact that Applicants are unable to determine *a priori* which targets are able to interact with the structurally undefined "fragment" or "CTBF" moieties shouldn't be regarded as a virtue since this information (or lack thereof) provides no distinguishing characteristics and/or identifying features that would allow a person of skill in the art to recognize what is claimed. Furthermore, in also serves to confirm that fact that Applicants are claiming virtually an unlimited number of compounds and providing only minimal examples in support thereof (i.e., one oxime library). This is not "commensurate in scope" with the claims.

[9] Applicants argue, "claims 78-89 ... wherein the term 'fragments' has been recited

instead of the term 'candidate target binding fragments' ... is devoid of an alleged functional terminology ... Whether or not the moiety bonded to -S-S-R^8 is termed a candidate target binding fragment or simply a fragment is a (1) small, (2) organic molecule, (3) water soluble, and (4) bound to -SS-R8. Properties (1)-(4) are all structural, physical properties (not functional) that distinguish the claimed library from other materials" (e.g., 4/20/06 Response, page 11, last paragraph).

[9] The –SS-R8 formula does not describe the "fragment" portion of the molecule. Thus, element (4) is of no consequence. Furthermore, the alleged distinguishing features in elements (1)-(3) would not serve to distinguish the claimed molecules either since the term "small" as in element (1) is a "relative" term that is indefinite (see 35 U.S.C. § 112, second paragraph rejection below), and the elements (2) and (3) (i.e., water soluble organic molecules) would still read on a virtually infinite number of compounds that are not adequately supported by Applicants' one example of an oxime library. As stated above, when there is *substantial variation within the genus*, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05). Here, the variation within the genus would be enormous because, according to Applicants, the claims read on virtually an infinite number of water soluble organic molecules (or at least 600,000+ as set forth in the "typical" pharmaceutical company archives and 11 commercial venders, see above) that do not share any common properties (other than their ability to dissolve in water at some unspecified level (e.g., see 35 U.S.C. § 112, second paragraph rejections below). It is well settled that claiming only a result (e.g., ability to act as a candidate target) fails to satisfy the constitutional requisite of promoting the progress of science and the useful arts since this seeks to monopolize all possible ways to achieve a given result (i.e.,

every conceivable library), far beyond those means actually discovered or contemplated by the inventor (i.e., oxime library), so that others would have no incentive thereafter to explore a field already fully dominated. *O'Reilly v. Morse*, 15 How. 62, *In re Fuetterer*, 50 CCPA 1453, 1963 C.D. 620, 795 O.G. 783, 319 F.2d 259, 138 USPQ 217; *Siegel v. Watson*, 105 U.S. Appl. D.C. 344, 1959 C.D. 107, 742 O.G 863, 267 F.2d 621, 121 USPQ 119.

Accordingly, the written description rejection cited above is hereby maintained.

6. Claims 53 and 67-89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

A. Claims 53 was amended in the August 19, 2005 Response (and again in the April 20, 2006 Response). However, the Examiner cannot find support for these amendments. For example, the Examiner does not find support for Applicants currently claimed subgenus of compounds that links an alkyl chain of 1 to 10 carbon atoms that is substituted with an amino group to an organic molecule. In addition, the Examiner doesn't find support for the "heterocyclic" groups further used to define this moiety as in, for example, claims 68, 69, 73, 74, 80, 81, 85 and 86.

Response

7. Applicant's arguments directed to the above New Matter rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for

the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue in the "remarks" and "priority" sections of their last response "Claim 53 has been amended to delete the phrase 'an organic molecule less than 2000 daltons and comprises a homocyclic aromatic radical, a heterocyclic aromatic radical or a heterocyclic radical,' which was the basis of the new matter rejection. Instead claim 53 now recites the term 'small organic molecule' which has been examined in previous claim amendments, without being rejected" (e.g., see 4/20/06 Response, page 7, paragraph 1); see also page 8, paragraph 1, "applicants have overcome the new matter rejection").

This is not found persuasive for the following reasons:

The Examiner respectfully disagrees. Applicants' have mischaracterized the basis of the rejection. While the Examiner certainly pointed to the "homocylcic aromatic radical ..." limitation above, this was merely exemplary and certainly not the only basis for rejection (e.g., see 10/20/05 Final rejection, pages 20 and 21, New Matter rejection, "For example, Applicants state that support can be found in at page 33, lines 26-33 for the currently claimed 'homocyclic aromatic radical, a heterocyclic aromatic radical or a heterocyclic radical' (e.g., see 8/19/05 Response, page 4, paragraph 1).". Specifically, Applicants failed to appreciate the "alkyl chain of 1 to 10 carbon atoms" limitation in the "additional" statement at the bottom of the rejection, "In addition, the Examiner does not find support for Applicants currently claimed subgenus of compounds that links an alkyl chain of 1 to 10 carbon atoms that is substituted with an amino group to an organic molecule less than 200 daltons and comprises a homocyclic aromatic radical,

a heterocyclic aromatic radical or a heterocyclic radical" (see original rejection and also newly amended rejection above). Here, the Examiner maintains that no support exists for this limitation in the specification and/or priority documents (see above).

Furthermore, the dependent claims still contain the objectionable language cited by Applicants (e.g., see claims 68, 69, 73, 74, 80, 81, 85 and 86 wherein the term heterocyclic is still used to define the CTBFs).

Accordingly, the New Matter rejection cited above is hereby maintained.

Claims Rejections – 35 U.S.C. 102/103

8. Claims 53, 67-69, 71-74, 78-81, 83-86, 88 and 89 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Erlanson et al. (Erlanson, D. A.; Braisted, A. C.; Raphael, D. R.; Randal, M.; Stroud, R. M.; Gordon, E. M.; Wells, J. A. "Site-directed ligand discovery" *PNAS* **August 2000**, *97(17)*, 9367-9372).

For ***claims 53 and 78***, Erlanson et al. (see entire document) teach the formation of a library of 8-15 disulfides with the requisite CTBF-SS-R^8 formula or fragment-SS-R^8 (e.g., see abstract; see also page 9368, column 2, paragraph 2, "In a typical experiment, … a library of 8-15 disulfide containing compounds is added to … protein-containing buffer"; see also see figure 1 wherein a library of R-C(=O)-NH-CH_2-CH_2-S-S-CH_2-CH_2-NH_2 compounds are disclosed with CTBF = "R-C(=O)-NH-CH_2-CH_2-" and R^8 = -CH_2-CH_2-NH_2; see also figure 3 showing different CTBF molecules containing homocyclic aromatic and heterocyclic rings; see also page 9367, column 1, paragraph 2, "We have developed an alternative strategy to rapidly and reliably identify small soluble drug

fragments (molecular weight ~ 250 Da) that bind with low affinity to a specifically targeted site on a protein or macromolecule [i.e., a CTBF]").

For ***claims 67, 79***, Erlanson et al. disclose a library wherein the CTBFs are small organic molecule of less than about 750 daltons (e.g., see page 9367, column 1, paragraph 2, "We have developed an alternative strategy to rapidly and reliably identify small soluble drug fragments (molecular weight ~ 250 Da) that bind with low affinity to a specifically targeted site on a protein or macromolecule [i.e., a CTBF]").

For ***claims 68, 73, 80, 85***, Erlanson et al. disclose, for example, amides (e.g., see figures 1 and 2).

For ***claims 69, 74, 81, 86***, Erlanson et al. disclose, for example, aromatic compounds and heterocyclic compounds (e.g., see figures 2 and 3).

For ***claims 71, 72, 76, 77, 83, 84, 88, 89***, Erlanson et al. disclose 1,200 compounds (e.g., see figure 1, "In the present case, 1,200 compounds were screened against TS in pools of 8 to 15 compounds"). Furthermore, it is clear that the mere scaling up of a prior art process capable of being scaled up would not establish patentability in a claim to an old process so scaled *In re Rinehart*, 531 F.2d. 1048, 189 U.S.P.Q. 143 (C.C.P.A. 1976).

The product of Erlanson et al. meet all of the structural limitations of the claimed product (see above) except for the product-by-process limitations (i.e., "combining" the library members together) and thus would either anticipate or render obvious the claimed library. See MPEP § 2113, "'[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself.

The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.' *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)." Here, Applicants' claims are drawn to a library of candidate target binding fragments (i.e., a product), but are defined by various method steps that produce said library (i.e., combining the library members together) and, as a result, represent product-by-process claims. Thus, the process limitations do not appear to provide any patentable weight to the claimed invention in accordance with MPEP § 2113. One of ordinary skill would expect the product to be the same no matter how it was "combined" together.

Response

9. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue, "applicants are entitled to a priority date of March 26, 1999, which is the filing date of the parent CIP application. Accordingly, the rejections of the outstanding office action ... for anticipation/obviousness are rendered moot" (e.g., see 4/20/06 Response, page 8, paragraph 1).

This is not found persuasive for the following reasons:

Applicants have only been afforded priority to the presently filed application (e.g., see priority section above) and, as a result, Applicants' arguments are moot.

Accordingly, the 35 U.S.C. § 102/103 rejection is hereby maintained.

New Rejections/Objections

Objections to the Claims

10. Claim 68, 73, 80, 84 objected to because of the following informalities:

A. For ***claims 68, 73, 80 and 84***, the word "hyiazines" in line 4 is misspelled. Correction is requested.

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 53 and 67-89 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an CTBF-S-S-R8 library wherein said CTBF represents an oxime, does not reasonably provide enablement for any CTBF and/or fragment as currently claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the

enablement requirement and whether any necessary experimentation is "undue". Some of these factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: Applicants' newly amended claims are directed to a broad genus of candidate target binding fragments (CTBF's) and/or just plain fragments (as set forth in newly added independent claim 78). Although Applicants' claims have been amended to recite "small" molecules that are "sufficiently soluble" to be test, the claimed CTBF's still read on virtually an infinite number of compounds because Applicants' do not limit the way in which the organic atoms can be arranged to form the claimed compounds. In addition, Applicants do not specify any target molecule or method of testing (e.g., see 35 U.S.C. § 112, second paragraph "metes and bound" rejection). Furthermore, Applicants admit that their claimed compounds read on at least 600,000+ compounds as set forth in "typical" pharmaceutical archives and as sold by various commercial vendors (e.g., see 4/20/06 Response, page 11, paragraphs 1 and 2). In addition, Applicants do not specify any target molecule or method of testing (e.g., see 35 U.S.C. § 112, second paragraph "metes and bound" rejection; see also 4/20/06 Response, page 11, section E, "E. Binding Properties

Would not Have Had to be Known A Priori in order for the Skilled Artsian to Recognize the Claimed Library"). Consequently, the nature of the invention cannot be fully determined because the invention has not been defined with particularity.

(3 and 5) The state of the prior art and the level of predictability in the art: The prior art indicates that it would be physically impossible to "make" all or even a substantial portion of the currently claimed libraries. For example, Lauf et al. state, "The preparation of new materials with novel and useful chemical and/or physical properties is at best unpredictable considering current levels of understanding. Consequently, the discovery of new materials depends largely on the ability to synthesize and analyze new compounds. Given approximately 100 elements in the periodic table, which can be used to make compositions consisting of three, four, five, six or more elements, the universe of possible new compounds remains largely unexplored" (e.g., see U.S. Patent Application No. 2004/0062911 A1, page 1, paragraph 4). In addition, Young et al. state, "For a given [combinatorial] reaction or sequence of reactions, the number of possible products can be astronomical ... it is impossible to make all possible products. Even with a two-component reaction with a modest number of building blocks, it generally does not make economic sense to build all the products, as there may be more than can be afforded and many may be largely redundant" (see Young et al., "Design of Diverse and Focused Combinatorial Libraries Using an Alternating Algorithm" *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 1916-1921, especially page 1916, column 1, paragraphs 1 and 2).

The prior art also indicates that not all libraries are created equal and that a person of skill in the art cannot predict whether "useful" results can be obtained by screening

any given library. For example, Muegge states, "the success rate of these early random libraries is considered to be low. The somewhat disappointing performance can be attributed, for example, to the high flexibility of synthesized molecules as well as to their high lipophilicity. In addition, the libraries were often limited in their pharmacophore diversity ... For receptor and enzyme targets, on average one lead compound is identified for 120,000 compounds screened. HTS is much less successful for targets of protein protein interaction" (e.g., see Muegge, "Pharmacophore Features of Potential Drugs" Chem. Eur. J. 2002, 8, No. 9, pages 1977-1981, especially page 1977, column 1, paragraph 1). In addition, this "disappointing" success rate is further plagued by "false positives" that "inflate" the true hit rate. For example, McGovern et al. state, "screening hit lists [i.e., libraries] continue to be populated, even dominated, by compounds that act with atypical properties that cannot be described by any existing model; such compounds are unlikely to be pharmaceutically useful" (e.g., see McGovern et al., "A Common Mechanism Underlying Promiscuous Inhibitors from Virtual and High-Throughput Screening" *J. Med. Chem.* **2002**, *45*, 1712-1722, especially page 1712, column 2, paragraph 1; see also page 1720, column 2, paragraph 2, "such nonspecific inhibitors would artificially inflate hit rates in screening for new drug leads. Much effort can be wasted chasing [these compounds] ... that are unlikely to be useful biologically"). This is also confirmed by Gilllet et al. state, "early results from combinatorial libraries were disappointing with libraries either failing to deliver the improved hit rates that were expected or resulting in hits that did not have "druglike" characteristics. Thus, it is now evident that diversity alone is an insufficient criterion for library design and other factors

should also be taken into account. For example, the physicochemical properties of the molecules that determine effects such as ADME are important as well as other factors such as cost and availability of reactants. Consequently, the focus in combinatorial library design has now shifted toward designing libraries based on a number of properties simultaneously" (e.g., see Gillet et al., "Combinatorial Library Design Using a Multiobjective Genetic Algorithm" *J. Chem. Inf. Comput. Sci.* **2002**, *42*, 375-385, especially page 375, column 1). In addition, even if a biologically active library member could be found, most never would be considered a "successful" drug candidate because many are eliminated for toxicity and safety issues, poor pharmacokinetics, and unfavorable physiochemical profiles (e.g., see Harter et al., "Estimation of Physiochemical and ADME Parameters" Handbook of Combinatorial Chemistry. Drugs, Catalysts, Materials. Vol. 2. Edited by D.C. Nicolaou, R. Hanko, and W. Hartwig 2002, Wiley-VCH Weinheim, pages 743-760, especially page 744, paragraph 1). Thus, much work would still be required to see if an "initial" library would actually be useful.

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: In contrast to the broad scope of the claims, Applicants' specification provides only one working example of a CTBF drawn to a cross-linked oxime library that inhibits the interaction between gp120 and CD4 (e.g., see specification, pages 76-84, Example 1, see also figures 2 and 4 wherein the aldehyde precursors to the oxime library are disclosed; see also figure 6).

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991).

12. Claims 78-89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

A. Claim 78 was added in the 4/20/06 amendment. However, to the extent that the term "candidate target binding fragment" has been broadened by removal of the words "candidate target binding", such increased breadth represents new matter. Therefore, claim 78 and all-dependent claims represent new matter.

Response

13. To the extent that Applicants' arguments can be applied to the new rejection set forth above, the following is noted:

Applicants argue, "New claims 78-89 recite 'fragment' instead of 'candidate target

binding fragment.' The word 'fragment; finds support from the phrase 'candidate target binding fragment.'" (see 4/20/06 Response, page 7, second to last paragraph) .

This is not found persuasive for the following reasons:

The word "fragment" is not limited to fragments that are used for target binding as set forth in the specification (e.g., see specification, page 15, middle paragraph). If this were not the case, then there would be no reason to use the words "candidate target binding" to modify the word fragment or set forth a definition (e.g., page 15, middle paragraph) in the specification. Furthermore, in the alternative, that "candidate target binding fragment" and "fragment" were identical in meaning (which is not the case, see above), use of this "inconsistent" terminology would still be objectionable as Applicants' would needlessly be using two different terms to describe the same thing. Therefore, Applicants' arguments are moot.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 53 and 67-89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claims 53 and 78**, the phrase "the CTBFs are sufficiently soluble in aqueous solutions to be tested for their ability to bind to a target biological molecule" is vague and indefinite. First, it is unclear what structure Applicants are referring to. The CTBF alone or, alternatively, the CTBF when it is attached to the -S-S-R^8 portion of the molecule

(i.e., to make the claimed CTBF-S-S-R^8 as set forth in the formula). If Applicants are referring to the CTBF alone then it is unclear what substituent is replacing the -S-S-R8 portion of the molecule that would necessarily have to be considered in any solubility determination. For example, CTBF-X may be soluble while CTBF-Y may not depending on the nature of X (hydrophilic) and Y (hydrophobic). Presumably a hydrophilic Y group could be used (e.g., large polyethyelene glycol) that would render any CTBF soluble in water rendering this test meaningless. If, on the other hand, Applicants are referring to the CTBF portion of the CTBF-S-S-R^8 molecule then, again, it is unclear how to judge the solubility of this fragment since its actual solubility is determined, at least in part, by the -S-S-R^8 portion of the molecule.

Second, it is unclear whether "insoluble" CTBFs would be considered "soluble" if they could be rendered soluble by the use of additives such as detergents or, perhaps, the target biological molecule itself. That is, the CTBFs alone would not be testable while the CTBFs when combined with various agents and/or target biological molecule would be?

Third, the phrase "sufficiently soluble" is a relative term that renders the claim indefinite (see MPEP 706.03(d)). The specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention because Applicants do not set forth the method that will eventually be used to "test" the solubility. In addition, techniques exist (e.g., solid state and/or solution phase NMR spectroscopy, a simple "weight" measurement) that would enable the "testing" of any target-ligand regardless of its

solubility rendering Applicants' claimed limitation meaningless (e.g., see Luca et al. "High-Resolution Solid-State NMR Applied to Polypeptides and Membrane proteins Acc. Chem. Res. 2003, 36, 858-865, especially abstract, "Solid-state NMR provides unique possibilities to study insoluble or noncrystalline molecules"). Thus, solution and solid phase techniques, for example, would enable the "testing" of "all" small molecule ligands regardless of solubility. Therefore, Applicants' implicit assertion that some "insoluble" ligands cannot be tested is simply inaccurate.

Consequently, the metes and bounds of the claimed invention cannot be determined. Therefore, claims 53, 78 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

B. The term "small organic molecule" in claims 53, 78 is a relative term, which renders the claim indefinite (see MPEP 706.03(d)). The term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Therefore, claims 53, 78 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

Response

15. To the extent that Applicants' arguments can be applied to the 35 U.S.C. § 112, second paragraph rejection denoted "B" above, the following is noted:

B. Applicants argue, "Instead claim 53 now recites the term 'small organic molecule' which has been examined in previous claim amendments, without being rejected" (e.g.,

see 4/20/06 Response, page 7, paragraph 1).

This is not found persuasive for the following reasons:

This is a false statement. The Examiner previously rejected the term "small organic molecule" as a "relative" term (e.g., see 5/19/05 Office Action, page 7, rejection denoted C, "The term "small" is a relative term [referring to small organic molecule], which renders the claim indefinite and/or unclear"). Therefore, Applicants' arguments are moot.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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November 10, 2006

JON EPPERSON, PH.D.
PATENT EXAMINER